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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 09/993,234
Filing Date: November 19, 2001
Appellant(s): ASHKENAZI, AVI J.

David Steffes
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed April 21, 2006 appealing from the Office action mailed March 24, 2006.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection under 35 U.S.C. 102(e) to be reviewed on appeal is correct.

Claim Rejections - 35 USC § 112, Withdrawn

The rejection of claim 34 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn. Claim 34 was rejected for new matter of the limitation "25-417" in line 2. However, this rejection is withdrawn because the specification at Figure 4 has support for amino acid residues 25-417 of SEQ ID NO: 6.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

6,153,402	Yu	11-2000

Exhibits A and B: a sequence alignment of the extracellular domains of DR3-V1 and Apo-3 at pages 6 and 7 of the appeal's brief, using BLAST 2 SEQUENCES downloaded from NCBI web site on 7/1/2006

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claim Rejections - 35 USC § 102

Claims 34 and 36-39 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,153,402 (Yu *et al.*; earliest priority dates is March 12, 1996 to US Provisional Application 60/013,285, herein after the '285 application, which is attached as appendix with the appeal's brief filed on 4/21/2006, ,see pages 16-103 of doc. code AP.B., doc. date: 4/21/2006 in the IFW).

The claims are rejected because one member of the Markush group in the base claim 34 is drawn to an isolated nucleic acid encoding a Apo-3 polypeptide comprising amino acid residues 25 to 198 of SEQ ID NO: 6. The dependent claims 36-39 are drawn to vector, vector operably linked to control sequences recognized by a host cell, a host cell comprising the vector, and process of producing a polypeptide using the host cell comprising the vector, respectively.

U.S. Patent No. 6,153,402 teaches an isolated nucleic acid (i.e. SEQ ID NO: 3) encoding a polypeptide comprising amino acid residues 25 to 198 of the instant SEQ ID NO: 6 as demonstrated by the attached sequence alignment provided with the Office action mailed on 10/07/2003. The '285 application has support for the nucleic acid encoding the amino acid residues at page 67, and also has support for the vector, the host cell, and a method of producing a polypeptide (page 5, 2nd paragraph).

(10) Response to Argument

A. Claim 34 is supported by the disclosure in compliance with 35 U.S.C. 112, first paragraph, rejection withdrawn

The rejection of claim 34 under 35 U.S.C. 112, first paragraph is withdrawn because the specification at Figure 4 has support for amino acid residues 25-417 of SEQ ID NO: 6.

B. Claims 34 and 36-39 are not anticipated by U.S. Patent No. 6,153,402 under 35 U.S.C. 102(e)

Appellant statement at the first paragraph of page 5 regarding the priority is correct, i.e. the Provisional Application 60/013,285 filed March 12, 1996 is the priority document that antedates that priority date accorded to the appealed claims.

Beginning 2nd full paragraph at page 5, appellant argues that the polypeptides taught in the '285 application do not match with the polypeptide recited in claim 34. This argument is based on the three sequence alignments from 3rd paragraph of page 5 to top of page 8. Appellant uses the term "DR3-V1" in the appeal's brief to refer to SEQ ID NO: 2 encoded by SEQ ID NO: 1 as taught in the sequence listing part of the '285

application. The '285 application at pages 66-70 teaches that SEQ ID NO: 1 is 1783 base pair isolated nucleic acid encoding SEQ ID NO: 2 ("DR3-VI" in the appeal's brief), a polypeptide comprising 428 amino acid residues. The instant specification at Fig. 4 discloses an isolated nucleic acid encoding "SEQ ID NO: 6" recited in the appealed claims. In summary, the sequence comparison in the appeal's brief is the comparison between SEQ ID NO: 2 taught in the '285 application ("DR3-VI") and SEQ ID NO: 6 ("Apo-3") recited in claim 34.

The 1st alignment at the paragraph bridging page 5 and 6 is comparison of the two N-terminal signal peptide sequences, i.e. the amino acid residues 1-30 of SEQ ID NO: 2 (DR3-V1) vs. the amino acid residues 1-24 of "SEQ ID NO: 6" recited in claim 34 of the instant application.

As appellant points out, they are different. However, the differences in their respective signal peptides are not a relevant issue. The claimed invention is not rejected because of the N-terminal signal peptide. Note the Office action mailed on 10/7/2003, and the sequence alignment provided in the Office action.

Likewise, the 3rd sequence alignment beginning at the bottom of page 7 to top of page 8 is also irrelevant because the 102(e) rejection of record is not about whether the amino acid residues 338 to 417 of "SEQ ID NO: 6" is anticipated by the prior art of record.

Rather, the prosecution history (note previous Office actions mailed on 12/14/2004 and 10/7/2003) indicates that the claimed invention is rejected because an isolated nucleic acid encoding a polypeptide comprising amino acid residues "25-198" of

"SEQ ID NO: 6" as recited in the appealed claim 34 is anticipated by the isolated nucleic acid encoding amino acids 36 to 209 of SEQ ID NO: 2 of the '285 (note page 67). Note the sequence alignment mailed out with the first Office action on 10/7/2003.

The amino acid residue 30 to 215 of the '285 application (top line, "DR3-V1") and the amino acid 25 to 198 of the instant SEQ ID NO: 6 (bottom line, "Apo-3") are compared in the 2nd alignment from middle of page 6 to the top of page 7. This 2nd alignment is crucial to determine whether the appealed claims are anticipated by the prior art of record or art.

The comparison of the two sequences, from middle of page 6 to the top of page 7, shows that the amino acid residue 30 to 215 of the '285 application (top line, "DR3-V1") and the amino acid 25 to 198 of the instant SEQ ID NO: 6 (bottom line, "Apo-3") are dissimilar. However, this dissimilarity between the two sequences results from two errors appellant made in the sequence comparison. First error has to do with identity of the amino acid residue at position "25" and "198" of SEQ ID NO: 6. These residues are critical to determine whether or not the claims are anticipated by the prior art of record. The second error has to do with the comparison method used in the appeal's brief.

The sequence alignment mailed to appellant with the first Office action on 10/7/2003 is a search result of the amino acid residues 25 to 198 of SEQ ID NO: 6 (Apo-3), renumbered to 1-174 respectively in the search result printout; this shows that the amino acid at position 25 is Gln, not Gly as indicated in the appeal's brief. The sequence alignment also shows that the amino acid residue at position 198 is Arg, not Gln in the appeal's brief..

The instant specification at Fig. 4 discloses SEQ ID NO: 6 is a 417 amino acid residue polypeptide. The amino acid residues "25-198" of "SEQ ID NO: 6" recited in claim 34 lies between two underlined regions (i.e. the 1st underline representing the N-terminal signal peptide, and the 2nd underline representing the transmembrane domain). The first amino acid (position 25) after the first underline is Q (Gln), and the last amino acid residue (position 198) just before the second line is R (Arg).

Second, the comparison method appellant uses in the appeal's brief is not an art-recognized method of aligning two given sequences for local alignment, in this case, the alignment of two extracellular domains of DR3-V1 and Apo-3. For example, the instant specification at Fig. 2 uses an alignment of several extracelluar domains of similar family of proteins. The disclosure at Fig. 2 of the instant specification uses the art-accepted parameters, i.e. extension and open gap penalties are permitted. The method used in the appeal's brief does not allow the art-accepted parameters.

Exhibit A is an art-accepted sequence alignment tool called Blast 2 Sequences available at the world wide web ncbi.nlm.nih.gov downloaded on 7/1/2006. Sequence 1 box contains the amino acid residue 30 to 215 the '285 application (top line, "DR3-V1") at the paragraph bridging pages 6 and 7 of the appeal's brief, formatted to FASTA, which is one letter code for each amino acids. This kind of code is used at Fig. 4 of the instant application. Sequence 2 box of Exhibit A is the corrected "25-198" of "SEQ ID NO: 6" (i.e. Gln at position 25, and Arg at position 198) as shown at Fig. 4 of the instant specification.

Exhibit B is the result of the alignment using the parameters shown in Exhibit A. Exhibit B demonstrates that the only difference between the extracellular domain of DR3-V1 and that of Apo-3 is that the extracelluar domain of DR3-V1 is longer than that of Apo-3. In other words, the extracelluar domain of DR3-V1 has 6 extra amino acid residues at its N-terminus, and another 6 extra amino acid residues at its C-terminus as compared to the extracellular domain of Apo-3. However, the amino acids 25 (renumbered to 1 in the query result) to amino acids 198 (renumbered to 174 in the query result in Exhibit D) of Apo-3 are identical to the amino acid residue 36 (renumbered to 7 in the query result) to amino acid residue 215 (renumbered to 180 in the query result). In summary, the extracellular domain of DR3-V1 comprises the amino acid residue sequences comprising the extracellular domain of Apo-3 (amino acid residue 25 to 198 of the instant SEQ ID NO:6).

Thus, appellant's argument that the extracellular domains of two polypeptides are different, is not persuasive. The dissimilarity as shown in the appeals brief is due to a result of errors in the amino acid composition of SEQ ID NO: 6 recited in claim 36 and also due to the comparison method not recognized in the art.

Beginning bottom of page 8, appellant argues the '285 application discloses no fragments having likeness to the Apo-3 polypeptide of the present claims. This argument is not persuasive because, as the Exhibit B, shows that amino acid residue 36 (renumbered to 7 in the query result) to amino acid residue 215 (renumbered to 180 in the query result) is identical to the amino acids 25 (renumbered to 1 in the query result) to amino acids 198 (renumbered to 174 in the query result).

Appellant also argues that "the Examine may have relied on such alteration in the deduced DR3-V1 polypeptide, and comparison of amino acid 36 with a portion of the Apo-3 polypeptide of the present claims appears to be impermissibly based either on the knowledge of the sequence of the present claims or the disclosure of Yu et al, which was not included in the '285 application." Appellant argues that such an alignment of sequences beginning at amino acid position number 36 does not involve any region of interest identified in the '285 application. Appellant argues that the '285 application provides no indication that a region of the deduced DR3-V1 polypeptide starting at amino acid position no. 36 exists as a separate polypeptide, begins a region of interest in the DR3-V1 polypeptide (i.e. extracellular domain), or has any significance whatsoever.

These arguments are fully considered but found unpersuasive, because the '295 application indeed discloses a sequence identical to the amino acids 25 to 198 of SEQ ID NO:2 recited in claim 34. An impermissible knowledge of the Examiner was not exercised to arrive at the identity of the amino acids or the identity of the nucleic acids that are identical to the claimed species (nucleic acid encoding a polypeptide comprising amino acid residue 25 to 198 of SEQ ID NO: 6 in claim 34) in the claimed invention. The computer program in the Patent Office searched whether any isolated nucleic acid encoding amino acid residue 25 to 198 of the instant SEQ ID NO: 6 was deposited in the patent data base, and the deposited sequence, which was Yu et al., claiming priority to the '285 application was generated.

Beginning the 2nd full paragraph of page 9 to page 10, appellant argues that SEQ ID NO: 2 in Yu et al., and SEQ ID NO: 2 in the '285 are different. This argument has been fully considered but found unpersuasive because only relevant issue based on the 102(e) rejection of record is whether the '285 application has support for a nucleic acid encoding the amino acid 25 and 198 of the instant SEQ ID NO: 6.

As applicant points out in the comparison of the two extracellular domains at the paragraph bridging pages 6 and 7, the '285 application has support for the amino acid 25 to 198 of SEQ ID NO: 6. In addition, page 67 of the '285 application shows that the isolated nucleic acid encoding amino acid residue 36 to 215 of SEQ ID NO: 2 (which is identical to amino acid 25 to 198 of SEQ ID NO: 6 in claim 34). Thus, SEQ ID NO: 1 as shown at page 67 of the '285 application anticipates the claimed invention of the isolated nucleic acid encoding a polypeptide comprising amino acid residue 25 to 198 of SEQ ID NO: 6, because the sequence in the '285 application comprises a nucleic acid encoding polypeptide comprising amino acid 36 to 215 of SEQ ID NO: 2, which is identical to the amino acid 25 to 198 of the instant SEQ ID NO: 6. For this reason, the rejection of record should be affirmed.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejection under 35 U.S.C. 102(e) should be sustained.

Respectfully submitted,

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Art Unit 1642

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Exhibit A

NCBI Entrez BLAST 2 sequences BLAST Example Help

BLAST 2 SEQUENCES

This tool produces the alignment of two given sequences using BLAST engine for local alignment.
The stand-alone executable for blasting two sequences (bl2seq) can be retrieved from NCBI ftp site
Reference: Tatiana A. Tatusova, Thomas L. Madden (1999), "Blast 2 sequences - a new tool for comparing protein and nucleotide sequences", FEMS Microbiol Lett. 174:247-250

Program blastp Matrix Not Applicable

Parameters used in BLASTN program only:
Reward for a match: **Penalty for a mismatch:**

Use Mega BLAST Strand option Both strands View option Standard

Masking character option X for protein, n for nucleotide Masking color option Black

Show CDS translation

Open gap 11 and extension gap 1 penalties
gap x_dropoff 50 expect 10.0 word size 3 Filter Align

Sequence 1

Enter accession, GI or sequence in FASTA format from: 0 to: 0

```
llgaraqggtrsprcdcagdfhkkiglfccrgcpaghylkapctepcgnstclvcpqdt
flawenhhnsecarcqacdeqasqvalencsavadtrcgckpgwfvecqvsqcvsssp f
ycqpcldcgalhrhtrllcsrrdtdcgtclpgfyehgdgcvscptstlgscpercaavc
gwrcaavcawrqmftv
```

or upload FASTA file Browse...

Sequence 2

Enter accession, GI or sequence in FASTA format from: 0 to: 0

```
qggtrsprcdcagdfhkkiglfccrgcpaghylkapctepcgnstclvcpqdtflawen
hhnsecarcqacdeqasqvalencsavadtrcgckpgwfvecqvsqcvsssp fycqpcl
dcgalhrhtrllcsrrdtdcgtclpgfyehgdgcvscptstlgscpercaavcgwr
```

or upload FASTA file Browse...

Align Clear Input

Comments and suggestions to blast-help@ncbi.nlm.nih.gov

Blast 2 Sequences results

PubMed Entrez BLAST OMIM Taxonomy Structure

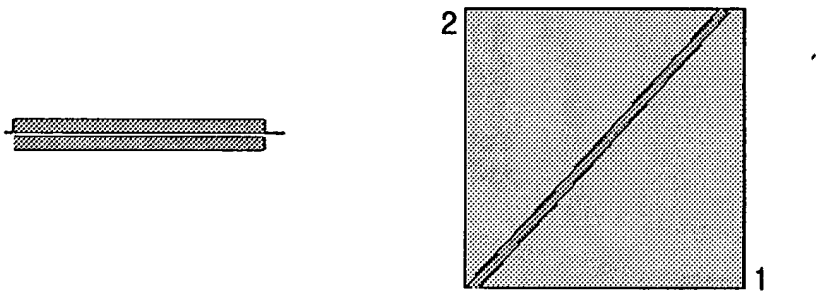
BLAST 2 SEQUENCES RESULTS VERSION BLASTP 2.2.14 [May-07-2006]

Matrix BLOSUM62 gap open: 11 gap extension: 1
x_dropoff: 50 expect: 10.00 wordsize: 3 Filter View option Standard
Masking character option X for protein, n for nucleotide Masking color option Black

Show CDS translation Align

Sequence 1: lcl|1_seq_1
Length = 193 (1 .. 193)

Sequence 2: lcl|2_seq_2
Length = 174 (1 .. 174)



NOTE: Bitscore and expect value are calculated based on the size of the nr database.

Score = 404 bits (1038), Expect = 2e-111
Identities = 174/174 (100%), Positives = 174/174 (100%), Gaps = 0/174 (0%)

DR3-V1
~~Query~~ 7 QGGTRSPRCDCAGDFHKKIGLFCCRGCPAGHYLKAPCTEPCGNSTCLVCPQDTFLAWENH 66
APO-3 QGGTRSPRCDCAGDFHKKIGLFCCRGCPAGHYLKAPCTEPCGNSTCLVCPQDTFLAWENH
~~Sbjct~~ 1 QGGTRSPRCDCAGDFHKKIGLFCCRGCPAGHYLKAPCTEPCGNSTCLVCPQDTFLAWENH 60

Query 67 HNSECARCQACDEQASQVALENCSAVADTRCGCKPGWFVECQVSQCVSSSPFYCQPCLDC 126
HNSECARCQACDEQASQVALENCSAVADTRCGCKPGWFVECQVSQCVSSSPFYCQPCLDC
Sbjct 61 HNSECARCQACDEQASQVALENCSAVADTRCGCKPGWFVECQVSQCVSSSPFYCQPCLDC 120

Query 127 GALHRHTRLLCSRRDTDCGTCLPGFYEHGDGCVSCPTSTLGSCPERCAAVCGWR 180
GALHRHTRLLCSRRDTDCGTCLPGFYEHGDGCVSCPTSTLGSCPERCAAVCGWR
Sbjct 121 GALHRHTRLLCSRRDTDCGTCLPGFYEHGDGCVSCPTSTLGSCPERCAAVCGWR 174

Exhibit B

CPU time: 0.02 user secs. 0.00 sys. secs 0.02 total secs.

Lambda	K	H
0.327	0.138	0.522

Gapped

Lambda	K	H
0.267	0.0410	0.140

Matrix: BLOSUM62
Gap Penalties: Existence: 11, Extension: 1
Number of Sequences: 1
Number of Hits to DB: 821
Number of extensions: 360
Number of successful extensions: 3
Number of sequences better than 10.0: 1
Number of HSP's gapped: 3
Number of HSP's successfully gapped: 1
Length of query: 193
Length of database: 1,302,931,322
Length adjustment: 126
Effective length of query: 67
Effective length of database: 1,302,931,196
Effective search space: 87296390132
Effective search space used: 87296390132
Neighboring words threshold: 9
X1: 15 (7.1 bits)
X2: 129 (49.7 bits)
X3: 129 (49.7 bits)
S1: 40 (21.7 bits)
S2: 74 (33.1 bits)